REMARKS

Status of the Claims

Claims 12-26 are pending in the present application. Claims 20-22 and 24 are withdrawn as directed to a non-elected invention. Claims 1-11 were previously canceled. Claim 12 is amended to cancel the phrase "under conditions." Claim 18 is amended to clarify that the ratio of the described cells is 1:1 to 1:10. Support for this amendment is found throughout the application as originally filed including, *e.g.*, on page 3, lines 23-26 and page 9, lines 1-4. Further, claim 18 specified this ratio in the preliminary amendment filed on June 22, 2006. Accordingly, no new matter is entered by way of this amendment. Entry of the amendment is respectfully requested since it does not raise new issues and/or reduces issues for appeal. Reconsideration is respectfully requested.

Issues Under 35 U.S.C. § 112, Second Paragraph

Claims 12-19, 23, 25, and 26 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for recitation of the phrase, "under conditions wherein said bone marrow cells or cord blood-derived cells are induced to differentiate into myocardial precursor cells and/or myocardial cells." Specifically, the Examiner states that it is unclear what the conditions are. Applicants respectfully traverse.

Although Applicants do not agree that the claims are unclear, in an effort to expedite prosecution, claim 12 is amended to cancel the phrase "under conditions." Further, claim 18 is amended to specify "a ratio of 1:1 to 1:10." Accordingly, the claims are not indefinite. Withdrawal of the rejections is respectfully requested.

Issues Under 35 U.S.C. § 103(a)

Claims 12-19, 23, 25, and 26 remain rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. 2002/0142457 to Umezawa *et al.* ("Umezawa") in view of Rangappa *et al.*, *Ann. Thorac. Surg.*, 2003, 75:775-779 ("Rangappa"), Egger *et al.*, *Nature*, 2004, Bonnet *et al.*

Clin. Exp. Med., Gilmore *et al. Exp. Hematol.*, 2000, and Lee *et al.*, *Blood*, 2004, for the reasons of record, *see* Office Action, pages 6-12. Applicants respectfully traverse.

The Examiner believes that an ordinary artisan would have been motivated to combine the bone marrow or cord blood derived multipotential stem cells described in Umezawa with the fat-derived stem cells of Rangappa to induce myocardial differentiation and achieve Applicants' invention. The Examiner makes this assertion because he believes that the method of differentiating bone-marrow or cord blood-derived stem cells into cardiomyocytes, as described in Umezawa, is identical to the method of differentiating the fat-derived stem cells, as described in Rangappa. According to the Examiner, since both bone marrow stem cells and fat-tissue derived stem cells can be differentiated into cardiomyocytes upon treatment with 5-azacytidine, an ordinary artisan would have been motivated to combine the two stem cell populations. Although the Examiner's reasoning for combining the two cell populations is different from those of the Applicants, the same result would allegedly be achieved, *i.e.*, bone marrow stem cells would predictably differentiate into cardiomyocytes, *see* Office Action of June 30, 2009.

A rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art, see *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395 (2007). However, if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Umezawa teach that cardiomyocytes may be used for heart regeneration or to treat heart disease, *see* paragraph [0151] to [0153] of Umezawa. For example, Umezawa indicate that bone marrow stem cells, which differentiate into sinus node cells, may be useful for therapeutic purposes, *see* paragraph [0153]. Rangappa indicate that differentiated cardiomyoctyes may be used for transplantation into the heart, *see* page 779 of Rangappa, left column. Both Umezawa and Rangappa warn that different results can be obtained if the cells are not used after a certain point in differentiation. For example, if sinus node cells are desired, further differentiation

should not be allowed to occur because the cells can subsequently differentiate into ventricular cardiomyocytes, *see* paragraph [0134] of Umezawa. Rangappa warns that if the cells are to be transplanted, transformation should occur within one week after differentiation to avoid dedifferentiation in the culture, *see* page 779 of Rangappa, left column.

However, the fat-derived stem cells described in Rangappa appear to differentiate into cardiomyocytes at a different rate than the bone marrow stem cells derived in Umezawa. Umezawa describe that under optimal conditions, *i.e.*, 3 μmol/l of 5-azacytidine, cells derived from bone marrow spontaneously beat two weeks after induction, *see* Example 1 of Umezawa and *see* Takakura Declaration, *enclosed.*

In contrast, fat-derived stem cells under optimal conditions, *i.e.* at 9 μmol/L of 5-azacytidine, spontaneously beat three weeks after induction, *see* pages 777-778, bridging paragraph. Accordingly, there would not be any motivation for an ordinary artisan to combine the stem cell populations into a single culture because the bone marrow stem cells could dedifferentiate or differentiate into another cell type by the time the fat-derived stem cells were at a stage useful for transplantation, rendering the bone marrow differentiated cells unsuitable for their intended purpose, *see* Takakura Declaration.

Further, an ordinary artisan could not have reasonably predicted that combining bone marrow stem cells and fat-derived stem cells, using known methods, *i.e.*, 5-azacytidine treatment, would have predictably resulted in the differentiation of both stem cell populations. Umezawa teaches that, optimally, 3 μmol/L of 5-acacytidine is used to differentiate bone marrow stem cells, *see* "best mode" described in Example 1 of Umezawa. Alternatively, Rangappa teaches that no transformation of fat-derived stem cells occurs at this 5-acacytidine concentration, *see* page 778, left column and Table 2 of Rangappa. Accordingly, the optimal conditions for transformation of bone marrow stem cell differentiation are different from the optimal conditions for differentiation of fat-derived stem cells. Based upon the foregoing, an ordinary artisan could not have reasonably predicted that conditions could be optimized such that both stem cell populations could have differentiated into cardiomyoctyes under the same conditions, rendering the reason for combining the two stem cell populations invalid, *see* Takakura Declaration.

Based upon the foregoing, Applicants submit that the Examiner's rationale for combining the two stem cell populations is not supportable. An ordinary artisan could not have reasonably expected that bone marrow stem cells and fat-derived stem cells could have been cultured at the same time and under the same conditions to obtain a useful cardiomyoctye population. The different rates of differentiation and different optimal culturing requirements would not have allowed an ordinary artisan to reasonably expect that such a result could have been achieved, *see also* Takakura Declaration.

The teachings Egger, Bonnet, Gilmore and Lee fail to remedy the deficiencies of Umezawa and Rangappa. These references are merely cited for describing the function of 5-azacytidine or to describe elements in the dependent claims. Accordingly, Applicants submit that the Examiner has not established a *prima facie* case of obviousness. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendment, remarks, and enclosed Takakura Declaration, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact L. Parker, Reg. No. 46,046, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: SEP 30 2009

Respectfully submitted,

By _____

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Attachment: Declaration under 37 C.F.R. § 1.132